it possible to stop or reduce alopecia, and especially to induce or stimulate hair growth and/or to increase hair density and/or to reduce hair loss.

Summary

In one aspect, the present invention refers to use of a peptide conjugate of formula (I) in the manufacture of a medicament for the treatment or the prevention of alopecia:

$A\text{-}X_1\text{-}X_2\text{-Pro-Ala-X-B}$

(I)

wherein:

- A represents a hydrogen atom, a C_6 to C_{20} acyl group or a cholesterol residue;
- X_1 represents a covalent bond, an alanine or a proline;
- X_2 represents an arginine, a lysine, or an alanine;
- X represents a lysine, an alanine, or a phenylalanine; and
- B represents a hydroxyl or an amine;

or one of its preferentially pharmaceutically, dermatologically or cosmetically acceptable salts.

In another aspect, the present invention refers to a process for manufacturing the peptide conjugate of formula (I) according to the present invention, characterized in that said process comprises the following successive steps:

a. synthesis, at least partially on solid support, of the peptide strand of formula $H\text{-}X_1\text{-}X_2\text{-Pro-Ala-X-B}$, wherein

- X_1, X_2, X are as defined according to the present invention and are suitably protected;
- B is the solid support or a suitably protected OH or NH_2 group;

b. optional grafting of group A onto the peptide strand of step (a) by acylation reaction, preferentially by the use of an activated acyl in the presence of a base;

c. deprotection of the protected amino acids optionally together with cleavage of the peptide from the resin, when B is a solid support;

d. optional purification of the peptide conjugate of formula (I) obtained, for example by HPLC; and

e. collection of the product of formula (I).

In yet another aspect, the present invention refers to a pharmaceutical, dermatological or cosmetic composition comprising at least one peptide conjugate of formula (I) as defined in the present invention, characterized in that it is a composition for the scalp.

The object of the present disclosure thus relates to a peptide conjugate of formula (I):

$$A\text{-}X_1\text{-}X_2\text{-Pro-Ala-X-B}$$

(I)

wherein:

- A represents a hydrogen atom, a C_6 to C_{20} acyl group or a cholesterol residue;
- X_1 represents a covalent bond, an alanine or a proline;
- X_2 represents an arginine, a lysine, or an alanine;
- X represents a lysine, an alanine, or a phenylalanine; and
- B represents a hydroxyl or an amine;

or one of its preferentially pharmaceutically, dermatologically or cosmetically acceptable salts.

The object of the present disclosure further relates to a process for manufacturing the peptide conjugate of formula (I) above, characterized in that said process comprises the following successive steps:

a. synthesis, at least partially on solid support, of the peptide strand of formula $H\text{-}X_1\text{-}X_2\text{-Pro-Ala-X-B}$, wherein
   - X_1, X_2, X are as defined above and (the reactive groups of which) are suitably protected;
   - B is the solid support or a suitably protected OH or NH_2 group;

b. optional grafting of group A onto the peptide strand of step (a) by acylation reaction (when it is desired that A is not a hydrogen atom), preferentially by the use of an activated acyl in the presence of a base;

c. deprotection of the protected amino acids optionally together with cleavage of the peptide from the resin, when B is a solid support;

d. optional purification of the peptide conjugate of formula (I) obtained, for example by HPLC; and

e. collection of the product of formula (I).

Moreover, the object of the present disclosure relates to a cosmetic use of a peptide conjugate of formula (I) as defined herein for reducing hair loss and/or stimulating hair growth.

Another object of the present disclosure relates to a pharmaceutical, cosmetic or dermatological treatment method for combating alopecia, and/or for stimulating hair growth, comprising the administration to a patient of a peptide conjugate of formula (I) as defined herein.

More particularly, the object of the present disclosure relates to a treatment method as above, characterized in that the administration is carried out by applying to the scalp a composition comprising at least one peptide described above. Advantageously, the object of the present disclosure relates to a treatment method as above, characterized in that at least one peptide described above is combined with another dermatological active ingredient, for example which improves activity on hair regrowth and has been described for that activity.

Among these compounds, mention may be made of:

- minoxidil,
- nicotinic acid esters,
- 5α-reductase inhibitors, or
- another peptide with dermatological activity.

In particular, exemplary peptides with dermatological activities which can be combined with the peptides according to the present disclosure include those found in application PCT WO97/18239 or WO2005/009456 for these particular examples.

The object of the present disclosure also relates to a peptide conjugate of formula (I) as defined herein, as medicinal product.

The object of the present disclosure thus relates to a peptide conjugate of formula (I) as defined herein, for dermatological use optionally in combination with another preferentially dermatological active ingredient, such as those which improve activity on regrowth and have been described for that activity, more particularly those cited above (minoxidil, nicotinic acid esters, 5α-reductase inhibitors and other peptides

with dermatological activity such as those found in application PCT WO97/18239 or WO2005/009456).

Equally advantageously, the present disclosure relates to a peptide conjugate of formula (I) as defined herein, for dermatological use, as sole active ingredient.

The present disclosure further relates to a peptide conjugate of formula (I) as defined herein, for use in the treatment or the prevention of alopecia.

In a complementary manner, the object of the present disclosure thus relates to a pharmaceutical, dermatological or cosmetic composition comprising at least one peptide conjugate of formula (I) as defined herein.

Definitions

"Peptide conjugate" / "Peptide strand"

The term "peptide" (equivalent to the term "oligopeptide") should be understood to mean polymers of amino acids, said amino acids being linked together by a peptide bond. A peptide bond is an amide bond linking two amino acids. A peptide generally contains between 2 and 80 to 100 amino acids, the upper limit not being clearly defined, but general relates to the domain of proteins. Thus, a "dipeptide" is a polymer fragment of two amino acids linked together by a peptide bond. A tripeptide is a polymer fragment of three amino acids linked together by a peptide bond, etc.

Within the context of the present application, the peptides or peptide conjugates are tetrapeptides (i.e., composed of 4 amino acids) or pentapeptides (composed of 5 amino acids).

When the expression "*peptide conjugate*", "*peptide strand*" or "*peptide fragment*" is used, these expressions simply refer to the succession of the amino acids concerned.

Conventionally, peptides (or proteins) can be extracted from a biological medium or manufactured synthetically. Preferably, the peptides according to the

Claims

1. Use of a peptide conjugate of formula (I) in the manufacture of a medicament for the treatment or the prevention of alopecia:

$A\text{-}X_1\text{-}X_2\text{-Pro-Ala-X-B}$

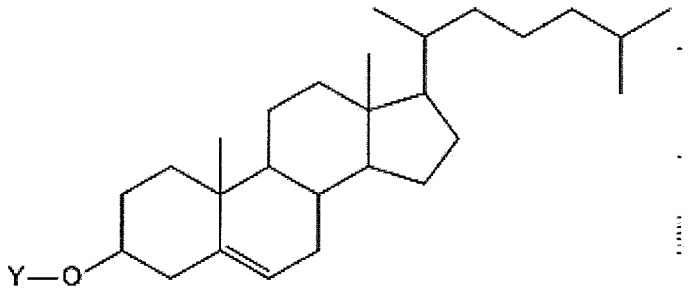
(I)

wherein:

- A represents a hydrogen atom, a C_6 to C_{20} acyl group or a cholesterol residue;
- X_1 represents a covalent bond, an alanine or a proline;
- X_2 represents an arginine, a lysine, or an alanine;
- X represents a lysine, an alanine, or a phenylalanine; and
- B represents a hydroxyl or an amine;

or one of its preferentially pharmaceutically, dermatologically or cosmetically acceptable salts.

2. The use according to claim 1, characterized in that group A represents a hydrogen atom, a C_{10} to C_{18} acyl group, preferentially a palmitoyl group, or a cholesterol residue according to formula (II):



(II)

wherein:

- Y represents the carbon atom of the ester bond between the cholesterol residue and X_1.

3. The use according to claim 1 or 2, characterized in that the salt is an acid addition salt, wherein the acid is for example hydrochloric acid, trifluoroacetic acid and/or acetic acid.

4. The use according to any one of claims 1 to 3, characterized in that X_1 is an alanine or a covalent bond, and X_2 is an arginine or an alanine.

5. The use according to any one of claims 1 to 4, characterized in that it is selected from:

- (1) H-Ala-Arg-Pro-Ala-Lys-OH,
- (2) Palm-Ala-Arg-Pro-Ala-Lys-OH,
- (3) Palm-Ala-Arg-Pro-Ala-Lys-NH_2,
- (4) Palm-Ala-Arg-Pro-Ala-Ala-NH_2,
- (6) Palm-Ala-Ala-Pro-Ala-Lys-NH_2,
- (7) Chol-Ala-Arg-Pro-Ala-Lys-NH_2,
- (8) H-Arg-Pro-Ala-Lys-OH, or
- (9) Palm-Arg-Pro-Ala-Lys-OH,

wherein

- Palm represents a palmitoyl group and
- Chol represents a cholesterol residue.

6. A process for manufacturing the peptide conjugate of formula (I) according to any one of claims 1 to 5, characterized in that said process comprises the following successive steps:

a. synthesis, at least partially on solid support, of the peptide strand of formula H-X_1-X_2-Pro-Ala-X-B, wherein

- X_1, X_2, X are as defined according to any one of claims 1 to 5 and are suitably protected;
- B is the solid support or a suitably protected OH or NH_2 group;

b. optional grafting of group A onto the peptide strand of step (a) by acylation reaction, preferentially by the use of an activated acyl in the presence of a base;

c. deprotection of the protected amino acids optionally together with cleavage of the peptide from the resin, when B is a solid support;

d. optional purification of the peptide conjugate of formula (I) obtained, for example by HPLC; and

e. collection of the product of formula (I).

7. The use according to any one of claims 1 to 5, wherein the medicament is for dermatological use in the treatment or the prevention of alopecia optionally in combination with another preferentially dermatological active ingredient.

8. The use according to any one of claims 1 to 5 characterized in that the alopecia is selected from androgenetic, congenital, acquired, localized, diffuse, acute or chronic alopecia.

9. A pharmaceutical, dermatological or cosmetic composition comprising at least one peptide conjugate of formula (I) as defined in any one of claims 1 to 5 and 7 to 8, characterized in that it is a composition for the scalp.

10. The composition according to claim 9 further characterized in that it is a composition for topical use.

11. The composition according to claim 9 or 10 characterized in that said composition comprises a peptide conjugate of formula (I) in the form of enantiomers and/or of diastereoisomers, preferentially the amino acids of the peptide conjugate being of L or D form exclusively or of L/D form.

12. The composition according to any one of claims 9 to 11 characterized in that said composition is selected from a lotion, a serum, a shampoo, such as a medicated shampoo, a spray, a gel or a cream such as a medicated cream.

13. The composition according to any one of claims 9 to 12 characterized in that said composition comprises at least one peptide of formula (I) according to any one of claims 1 to 5 at a concentration ranging between 10^{-9} and 10^{-4} mole/litre of composition, preferably between 10^{-7} and 10^{-5} mole/litre of composition.

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